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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/724,805	12/01/2003	Mark Edward Bunnage	PC10384B	5555

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PFIZER INC.  
PATENT DEPARTMENT, MS8260-1611  
EASTERN POINT ROAD  
GROTON, CT 06340

EXAMINER

MCKENZIE, THOMAS C

ART UNIT	PAPER NUMBER
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1624

DATE MAILED: 03/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

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## Office Action Summary

Application No.

10/724,805

Applicant(s)

BUNNAGE ET AL.

Examiner

Thomas McKenzie, Ph.D.

Art Unit

1624

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 14 December 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 18-30 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 24-26 is/are allowed.
- 6) ☒ Claim(s) 18-23 and 27-30 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date 12/3/03 & 12/14/04.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

1. This action is in response to amendments filed on 12/14/04. There are thirteen claims pending and thirteen under consideration. Claims 24-27 are compound claims. Claims 18-23 and 28-30 are method of making claims. This is the second action on the merits. Applicant has amended claims 18, 19, and 22-30. Claims 18-24 and 26-30 were previously rejected. Claims 24-26 were designated as containing allowable subject matter. The application concerns some intermediate compounds and processes of making compounds related to Sildenafil.

### ***Response to Amendment***

2. Applicants' amendment to the specification overcomes the objection made in point #3 of the previous office action. Applicants' amendments to the relevant claims overcomes the objections made in points #4-#8 of that action. Applicants' deletion of "general" from the claims overcomes the indefiniteness rejection made in point #9. Applicants' new proviso in claim 27 concerning the compound with R<sup>4</sup> = methyl or ethyl overcomes the art rejection over Macor ('368) made in point #11. However, that amendment creates a new matter rejection, which is discussed below.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-23 and 28-30 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for said dehydrogenation being carried out in the presence of a dehydrogenation agent selected from: palladium on carbon, palladium on carbon in the presence of a hydrogen acceptor and/or an acid, a high oxidation potential quinone, oxygen, MnO<sub>2</sub>, or triphenylmethanol in trifluoroacetic acid, does not reasonably provide enablement for all dehydrogenations. The specification does not enable any skilled process chemist or pilot-plant operator to make the invention commensurate in scope with these claims. “The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims”, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546.

a) Determining if any particular substrate would react under Applicants conditions would require synthesis of the substrate II and subjecting it to dehydrogenation with a an unknown list of oxidants, a large quantity of experimentation. b) The direction concerning dehydrogenating compound II is

found in line 20, page 4, and line 5, page 6, and line 20, page 7, which merely states Applicants intent to do so. The passage spanning line 5, page 12 to line 6, page 13 gives examples of intended reagents. c) There are two working example of dehydrogenating compound II. These are found lines 24-26, page 23 and lines 15-18, page 25. Both working examples involve the solid catalyst Pd/C. d) The nature of the invention is chemical synthesis, which involves chemical reactions. e) The state of the art is no list of reagents or reaction condition exists which teach every possible "dehydrogenation reaction". Such reactions and reagents will be limited by the chemical nature of the side chains embraced by radicals  $R^1$ - $R^4$ , as well as the oxidatively sensitive nitrogen atoms present in the mandatory piperazine and pyrazole rings in formula II. f) The artisan using Applicants invention to prepare the claimed compounds would be a process chemist or pilot plant operator with a BS degree in chemistry and several years of experience. He would know how to employ the reagents listed in passage spanning line 5, page 12 to line 6, page 13, but be unaware of how to devise additional ones.

g) Chemical reactions are well-known to be unpredictable, *In re Marzocchi*, 169 USPQ 367, *In re Fisher*, 166 USPQ 18. In addition, catalytic reaction, as exemplified by Applicants working examples, are inherently understood to be unpredictable, *MOBIL OIL CORPORATION v. W.R. GRACE & COMPANY*, 180

USPQ 418, *Merck & Co. v. Olin Mathieson Chemical Corp.*, 253 F.2d 156, 164, 116 USPQ 484, 490 (4th Cir. 1958), *Corona Cord Tire Co. v. Dovan Chemical Corp.*, 276 U.S. 358, 368-369 (1928), *Application of Grant*, 304 F.2d 676, 679, 134 USPQ 248, 250-251 (CCPA 1962); *Rich Products Corp. v. Mitchell Foods, Inc.*, 357 F.2d 176, 181, 148 USPQ 522, 525-526 (2d Cir. 1966), cert. denied 385 U.S. 821, 151 USPQ 757 (1966); *Ling-Temco-Vought, Inc. v. Kollsman Instrument Corp.*, 372 F.2d 263, 268, 152 USPQ 446, 450-451 (2d Cir. 1967); *Georgia-Pacific Corp. v. United States Plywood Corp.*, 258 F.2d 124, 132-133, 118 USPQ 122, 128-129.

h) The breadth of the claims includes all of the thousands of compounds of formula II as well as the presently unknown list of reactions embraced by the term "dehydrogenation reaction". Thus, the claims are broad.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' invention.

Applicants argue that the BS process chemist making Applicants' compounds "would have the knowledge of any number of standard dehydrogenation methods" and "would be extremely familiar with the various methods of dehydrogenation". This is not persuasive for two reasons. Firstly, although Applicants allege that such methods are well known, they fail to mention any, other than those of the working examples. Secondly, two standard undergraduate organic textbooks, Streitwieser (Introduction to Organic Chemistry, 2nd Ed.) and Roberts (Basic Principles of Organic Chemistry) list in their indices a total of three methods for such a dehydrogenation reaction as presently claimed. Streitwieser (Introduction to Organic Chemistry, 2nd Ed.) states that such reactions can be done catalytically or with sulfur. Roberts (Basic Principles of Organic Chemistry) lists selenium as the only such reagent. The graduate-level textbook House (Modern Synthetic Reactions) lists four basic methods. These methods are catalytic (palladium or Raney nickel), high oxidation potential quinones (chloranil tetrachloro-o-benzoquinone), selenium, and sulfur. Thus, the only standard methods not presently considered as enabled are selenium and sulfur. Are these the only additional dehydrogenation agents which Applicants intend to include or are there others? If so, where would that BS chemist find such agents?

4. Claim 27 is newly rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The proviso in the next two lines of claim 27 lacks description. Nowhere in the specification is such a relationship linking the description among radicals  $R^3$ ,  $R^4$ , and  $R^a$  described. Such a negative limitation requires description. In *Ex parte Grasselli, et al.* 231 USPQ 393, decided June 30, 1983, the U.S. Patent and Trademark Office, Board of Patent Appeals and Interferences said: "we agree with the examiner's position of record that the negative limitations recited in the present claims, which did not appear in the specification as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112." "It might be added that the express exclusion of certain elements implies the permissible inclusion of all other elements not so expressly excluded. This clearly illustrates that such negative limitations do, in fact, introduce new concepts."

***Allowable Subject Matter***

5. Claims 24-26 are allowed.

***Conclusion***

6. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for




reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

7. Information regarding the status of an application should be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at (866) 217-9197 (toll-free). Please direct general inquiries to the receptionist whose telephone number is (703) 308-1235.

8. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose

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telephone number is (571) 272-0670. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, please contact James O. Wilson, acting SPE of Art Unit 1624, at (571)-272-0661.

  
Thomas C. McKenzie, Ph.D.  
Primary Examiner  
Art Unit 1624